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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY/DOCKET NO.
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HM12/0226

SEARCHED	INDEXED	PAPER NUMBER
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1644

DATE MAILED:

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

Responsive to communication(s) filed on 12/4/98

This action is FINAL.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 months, or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(e).

Disposition of Claims

Claim(s) 1 - 83 is/are pending in the application.
Of the above, claim(s) 11 - 66, 68 - 82 is/are withdrawn from consideration.
 Claim(s) 1 - 10, 67, 83 is/are allowed.
 Claim(s) is/are rejected.
 Claim(s) is/are objected to.
 Claim(s) are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948. SUBSTITUTED
 The drawing(s) filed on _____ is/are objected to by the Examiner.
 The proposed drawing correction, filed on _____ is approved disapproved.
 The specification is objected to by the Examiner.
 The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 All Some* None of the CERTIFIED copies of the priority documents have been
received.
 received in Application No. (Series Code/Serial Number) _____
 received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e). SUBSTITUTED

Attachment(s)

Notice of Reference Cited, PTO-892
 Information Disclosure Statement(s), PTO-1449, Paper No(s). 4/5
 Interview Summary, PTO-143
 Notice of Draftsperson's Patent Drawing Review, PTO-948 SUBSTITUTED
 Notice of Informal Patent Application, PTO-152

-SEE OFFICE ACTION ON THE FOLLOWING PAGES-

DETAILED ACTION

1. The Art Unit location and the examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1644.
2. Applicant's election with traverse of Group I (claims 1-10, 67,83) and the species CD40 ligand in Paper No. 8 is acknowledged. The traversal is on the ground(s) that there are common search classifications; that certain groups are sufficiently connected in design, operation and effects as to provide for one practical and efficient search; and that there should be no serious burden on the examiner.

Applicant's arguments are not found persuasive because the inventions must be independent (see MPEP 802.01, 806.04, 808.01) or distinct as claimed (see MPEP 806.05-806.05(l))) for the reasons of record set forth in the Restriction Requirement (Paper No. 6). Also, the inventions require non-coextensive searches whether or not the classifications alone are coextensive.

The requirement is still deemed proper and is therefore made FINAL.

Claims 11-66, 68-82 and the non-elected species are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.
4. The oath or declaration is defective because it does not provide for 119(e) priority to the provisional application 60/032145.
5. Applicant should amend the first line of the specification to correct the serial number of the provisional application relied upon for priority. The serial number should be 60/032145
6. The Abstract of the Disclosure is objected to because it does not adequately describe the claimed invention. Correction is required. See MPEP 608.01(b).
7. The drawings submitted with this application were declared informal by the applicant. Accordingly, they have not been reviewed by a draftsperson at this time. When formal drawings are submitted, the draftsperson will perform a review.

Direct any inquiries concerning drawing review to the Drawing Review Branch (703) 305-8404.

8. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Applicant is reminded that it is required to identify the nucleotide and amino acid sequences in the specification with SEQ. ID NOS.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required

9. The following is a quotation of the first paragraph of 35 U.S.C. § 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
10. Claims 1-7, 67, 83 are rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are indefinite in the recitation of "an accessory molecule ligand" because the characteristics of the "ligand" are ambiguous and unclear. This language is vague and indefinite since it encompasses a myriad of molecules. Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies the "an accessory molecule ligand" encompassed by the claimed invention. While page 20 of the instant specification discloses that "an accessory molecule ligand" refers to members of TNF family; the art recognizes a number of different molecules that serve as "an accessory molecule ligand" (e.g. members of the B7 : CD28 family of costimulatory molecules). The recitation of "an accessory molecule ligand" fails to distinctly claim what that protein is and what the compositions are made up of. Further, it is noted that "ligand" can be considered a relative term in that with receptor-ligand interactions, whether a molecule is the ligand or the receptor can be a matter of perspective or point of reference (e.g. CD40 ligand is a ligand for CD40; CD40 is a ligand for CD40 ligand).

There is insufficient direction or guidance provided to assist one skilled in the art in the selection of "an accessory molecule ligand organic molecules" commensurate in scope with the claimed invention nor is there sufficient evidence provided that any "accessory molecule ligand" including all members of the disclosed TNF family could be used to alter the immunoreactivity of a cell including tumor cells. It would require undue experimentation to produce all such possible "accessory molecule ligands" without more explicit guidance from the disclosure. It would require undue experimentation to investigate all such "accessory molecule ligands". Applicant has failed to enable or provide written description for nucleic acids encoding a myriad of "accessory molecule ligands" and fails to provide sufficient guidance to those skilled generally on how to make and use "accessory molecule ligands", commensurate in scope with the claimed invention to alter immunoreactivity of cells. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. It appears that undue experimentation would be required of one skilled in the art to practice the claimed methods to alter immunoreactivity of cells with "accessory molecule ligands", commensurate in scope with the claimed invention.

The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- (c) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371[®] of this title before the invention thereof by the applicant for patent.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103[®] and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1-8, 10 and 83 are rejected under 35 U.S.C. § 102(b) as being anticipated by Yellin et al. (*J. Immunol.*, 1994). Yellin et al. teach that transfected cells, including leukemia cells, with CD40 ligand enhances a cell costimulatory activity, including the priming and clonal expansion of antigen specific T cells as well as providing helper function for cytotoxic T cell responses (see entire document, including the Abstract and Discussion). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed limitations are inherent properties of the referenced methods to increase the immunogenicity of cells including leukemic cells by modifying said cells to express CD40 ligand.

15. Claims 1-10 and 83 are rejected under 35 U.S.C. § 102(b) as being anticipated by Alderson et al. (*J. Exp. Med.*, 1993). Alderson et al. teach that CD40 ligand transfected cells induce monocytes to become tumorcidal against human melanoma cells, which indicated that the CD40 ligand had potent biological effects (see entire document, including the Abstract and Discussion). Alderson et al. Teaches transfection with either murine or human CD40 ligand (for example, see page 671). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed limitations are inherent properties of the referenced methods to increase the immunogenicity of cells including leukemic cells by modifying said cells to express CD40 ligand.

16. Claims 1-7, 67 and 83 are rejected under 35 U.S.C. § 102(e) as being anticipated by Freeman et al. (U.S. Patent No. 5,861,310) (see entire document). Freeman et al. teach altering the reactivity of a cell and treating human neoplasia by introducing a gene encoding an accessory molecule ligand (B7) alone or together, that is to be expressed on a cell surface, including tumor cells (see entire document). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed limitations are inherent properties of the referenced methods to increase the immunogenicity of tumor cells by modifying said cells to express B 7 molecules.

Although it is acknowledged that CD40 ligand is the elected species, this reference, which is used in the obviousness rejection below, anticipates the claimed methods.

17. Claims 1-10, 67 and 83 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Freeman et al. (U.S. Patent No. 5,861,310) in view of Yellin et al. (J. Immunol., 1994) and Alderson et al. (J. Exp. Med., 1993) as well as pages 40-53 of the instant specification.

The instant claims are drawn to methods of altering the immunoreactivity of human cells or treating human neoplasia by inserting CD40L

Freeman et al. teach altering the reactivity of a cell and treating human neoplasia by introducing a gene encoding an accessory molecule ligand (B7) alone or together, that is to be expressed on a cell surface, including tumor cells (see entire document). Freeman et al. differs from the instant elected invention by not disclosing CD40 ligand as a costimulatory or accessory molecule

Yellin et al. teach that transfecting cells, including leukemia cells, with CD40 ligand enhances a cell costimulatory activity, including the priming and clonal expansion of antigen specific T cells as well as providing helper function for cytotoxic T cell responses (see entire document, including the Abstract and Discussion).

Alderson et al. teach that CD40 ligand transfected cells induce monocytes to become tumoricidal against human melanoma cells, which indicated that the CD40 ligand had potent biological effects (see entire document, including the Abstract and Discussion). Alderson et al. Teaches transfection with either murine or human CD40 ligand (for example, see page 671).

Therefore, it would have been prima facie obvious to the ordinary artisan at the time the invention was made to substitute the potent costimulatory/accessory molecule properties of the CD40 ligand into the methods of Freeman et al. to alter the immunoreactivity of cells, that is, to increase antigen presentation and/or immunoreactivity. The claimed limitations encompassing chimeric genes and vectors were known and practiced by the ordinary artisan at the time the invention was made, as evidenced by Freeman et al. Pages 40-53 of the instant specification also acknowledges that the general methods of providing chimeric/gen therapy constructs as well as manipulating cells were known and practiced at the time the invention was made.

One of ordinary skill in the art at the time the invention was made would have been motivated to select CD40 ligand as an accessory molecule ligand to express in cells, including tumor cells, to increase their immunoreactivity. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Patent Examiner
Group 1640
Technology Center 1600
February 25, 1999

Philip Gambel